REVIEW ARTICLE

The Impact of Electromagnetic Fields on Female Fertility: A Scoping Review of Research Designs and Study Limitations

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ABSTRACT

Background: The modern lifestyle has heightened exposure risks to various forms of electromagnetic fields (EMFs). Exposure to EMF has been shown to impair cellular homeostasis, endocrine function, reproductive function, and foetal development in animal models. To assess the reproductive risks of EMFs in human, it is crucial to examine the research methodology used, in order to provide the most reliable risk estimations. This review paper evaluates the study designs employed to investigate the impact of EMFs on female fertility and addresses the limitations of the research methodologies. **Methods:** This review follows the Preferred Reporting Items for Systematic Review and Meta-Analysis Extension for Scoping Review (PRISMA-SCR) guidelines. Seven electronic databases were utilised to access recent cohort studies published between the years 2013 to 2023. **Results:** A total of 33 articles reporting on EMFs and fertility were analysed. Majority of the studies employed animal study design (n= 15), followed by 9 observational studies, 4 case-control, 3 in vitro studies and 2 interventional studies. Thematic analysis identified five main themes addressing the methodological limitations; (i) operationalisation, (ii) measurement and instrumentation, (iii) contextual constraints, (iv) practical constraints, and (v) analytical constraints. **Conclusion:** This review identifies several key limitations on the current research methodologies that can be incorporated into future studies to support the development of empirical study designs.

INTRODUCTION

Electromagnetic fields (EMFs) are invisible areas of energy that are categorised into non-ionising EMFs, which are typically harmless, and ionising EMFs, which have the potential to cause cellular and DNA damage (National Cancer Institute, 2022). The waves of EMFs are emitted by a diverse range of devices and technologies essential for modern life, facilitating communication, transportation, healthcare, and more. It encompasses a broad spectrum, ranging from extremely low frequency (ELF) waves produced by power lines to radiofrequency (RF) waves generated by mobile phones and microwaves (Gye & Park, 2012).

While these technologies offer significant benefits, concerns have been raised regarding their potential impacts on human health. Humans in modern society should be aware of the risks associated with EMFs, as exposure to diverse forms of EMFs is unavoidable in domestic and professional environments. Through *in vitro* and *in vivo* studies, EMF exposure adversely affects embryonic and foetal development (Pourlis, 2009), modifies endocrine hormones (Rodriguez et al., 2004), and disrupts gonadal functions (Guney et al., 2007; Kaur et al. 2023). The potential threats associated with EMFs exposure are contingent upon the intensity, wave type, duration, and frequency. Nevertheless, the findings regarding the hazards of EMF on human health remain uncertain due to the contradictory results, which could be attributed to the non-standardised methodologies and assessment tools. Furthermore, present studies primarily focused on epidemiology, and risk assessment, with insufficient data addressing study designs and their limitations.

Therefore, the main focus of this review is to evaluate the types of study designs employed to investigate the impact of EMFs exposure on female fertility and further analyse the limitations of the research methodologies from the selected studies. This review is based on the Preferred Reporting Items for Systematic Review and Meta-Analysis Extension for Scoping Review (PRISMA-SCR) guidelines. Unlike traditional systematic reviews, which address specific research questions, a scoping review aims to provide a broad overview of the literature, sources of evidence, and knowledge gaps.

To the best of the authors' knowledge, this is the first scoping review that provides analytical data on study designs, and limitations concerning the reproductive risks associated with low and high frequencies of EMF exposure in females. The findings from this review can assist policy makers and public health authorities in addressing

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potential risks concerning the use of EMF-emitting devices. This review will be beneficial for new authors to refine their knowledge and develop new research ideas by considering the limitations identified in this study. Above all, it is hoped to add to the existing body of knowledge and fills the gap in the current EMF literature.

MATERIALS AND METHODS

The Preferred Reporting Items for Systematic Review and Meta-Analysis Extension for Scoping Review (PRISMA-SCR) 2018 guidelines was employed throughout this review, comprising twenty essential reporting items and two optional items (Tricco et al., 2018). The protocol of this review was approved by the approving committee for the undergraduate research project (AHBS 3612) course of Department of Biomedical Science, Kulliyyah of Allied Health Sciences, IIUM.

Eligibility Criteria

Inclusion

i. Studies that evaluate the effects of EMF on general health and female infertility
ii. Studies published between 2013 and 2023.
iii. Studies that include qualitative and quantitative analyses.
iv. Studies that include experimental and observational designs.
v. Studies written in the English language.

Exclusion

Non-original articles, such as conference proceedings, abstracts, systematic reviews and meta-analyses.

Information Sources

A comprehensive literature search was conducted using the following electronic databases; PubMed, Google Scholar, ScienceDirect, Wiley Online Library, ProQuest, Cochrane and Scopus.

Search

The search in the databases was carried out using the following keywords search strategy: “electromagnetic fields”, “EMF”, “fertility”, “infertility”, “female infertility”, “health effects”, “reproduction”, “pregnancy”, “abortion” and “oocyte”. The Boolean terms (AND and OR) were also used to specify and separate each keyword, widening the search result and ensuring the keywords were present in the articles.

Study Selection and Data Collection Process

Two reviewers independently screened the titles and abstracts in accordance with the inclusion criteria. Following that, the full-text articles were further accessed for eligibility. Data from studies that meet all the eligibility criteria were recorded and analysed in the excel spreadsheet. Disagreements were resolved by discussion.

Data Items

Data extracted from each study include: (i) the study characteristics, (ii) the types of study design used, and (iii) study limitations. Thematic analysis was utilised to generate themes pertaining to the study limitations identified in the reviewed articles. The data was clustered as themes and subthemes according to the common pattern.

Methodological Quality Assessment

The quality of the selected articles in this review was assessed by two authors to ensure the validity and reliability of the research papers. However, a formal quality assessment using tool such as the Crowe Critical Appraisal Tool (CCAT) was not conducted, as it is not within the scope of the scoping review methodology (Pham et al., 2014). While this step is beneficial, it is optional in a scoping review since a detailed critical appraisal of study quality is often not the primary focus.

RESULTS

Study Selection

A total of 157 articles were identified for this review via seven electronic databases. Following the removal of 47 duplicates, 110 articles were selected for the screening process. The first screening phase involved evaluation of the titles, resulting in the exclusion of 4 articles. In the second phase, the titles and abstracts were screened and a total of 73 articles were excluded as they did not meet the inclusion criteria. In total, 33studies were identified as being eligible for full text evaluation (Figure 1).

Study Characteristics

Articles selected were published within the last ten years, from 2013 to 2023. The majority of the articles (n= 15) involved animal studies (Poulletier de Gannes et al., 2013; Hafizi et al., 2014; Bakacak et al., 2015; Qi et al., 2015; Ahmadi et al., 2016; Alchalabi et al., 2016a; Alchalabi et al., 2016b; Khaki et al., 2016; Shirai et al., 2017; Woelders et al., 2017; Papoyan et al., 2018; Saygin et al., 2018; Ruan et al., 2019; Burcu et al., 2020; Wang et al., 2022). A total of 9 studies conducted observational studies which included retrospective, prospective, longitudinal cohort and cross-sectional designs (de Vocht et al., 2014; de Vocht & Lee, 2014 secondary data; Abad et al., 2016; Xu et al., 2016; Li et al., 2017; Migault et al., 2018; Auger et al., 2019; Ingle et al., 2020; Tokinobu et al., 2021). Four studies collected data via case-control design (Mahmoudabadi et al., 2013; Mahmoudabadi et al., 2015; Sadeghi et al., 2017;

Esmailzadeh et al., 2019). Interventional study was performed in 2 studies (Rad et al., 2014; Dias et al., 2023), while in-vitro experimental study was conducted in 3 studies (Suzuki et al., 2017; Chen et al., 2021; Kozlowska et al., 2021). The study characteristics of the reviewed articles are presented in the Supplementary Table 1.

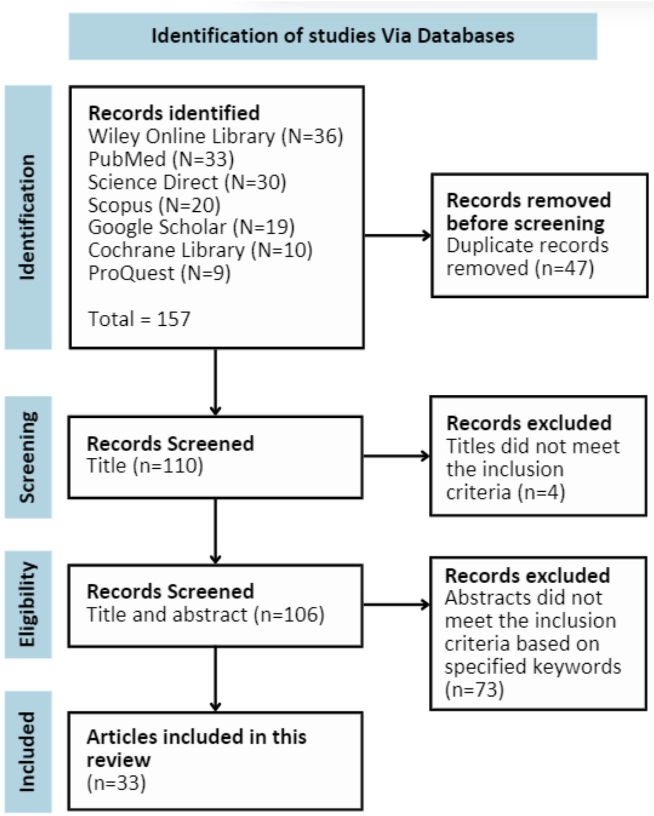

Figure 1: PRISMA flow diagram

Thematic Analysis

Based on the research question "*What are the study limitations identified in the selected studies*?", thematic analysis of the reviewed papers revealed five main themes addressing the methodological limitations of various study designs employed; (i) operationalisation, (ii) measurement and instrumentation, (iii) contextual constraint, (iv) practical constraint, and (v) analytical constraint (See Supplementary Table 1). The theme operationalisation implied three subthemes: (a) sample size, (b) duration of exposure, and (c) risk of bias. Measurement and instrumentation yielded two subthemes: (a) validity threats, and (b) limitations/variations in measurement methods. The contextual constraint mainly pertained to the applicability of findings in humans. Practical constraint was mainly related to resource constraints, which include lack of data availability and limited technical expertise. The analytical constraints were primarily related to the limitations of statistical analysis and the significance of the findings.

Theme 1: Operationalisation

<u>Sample size</u>

This review noted that all the study designs employed in the selected studies showed limitation of small sample size, which limits the generalisability of their findings to broader population or different context; such as interventional study design by Rad et al. (2014), and Dias et al., 2023; animal studies by Hafizi et al. (2014), Bakacak et al. (2015), Qi et al. (2015), Ahmadi et al. (2016), Khaki et al. (2016), Papoyan et al. (2018) and Saygin et al. (2018); and observational studies by Xu et al. (2016), Ingle et al. (2020) and Abad et al. (2016).

<u>Duration of exposure</u>

Three articles examining the impacts of EMF exposure on female fertility were identified using *in vitro* experimental study design. All three studies emphasised on the short-term EMF exposure, with a lack of long-term effects data. In a study by Suzuki et al. (2017), the short EMF exposure time may inadequately reflect the possible impacts on fertilisation and early embryonic development. Moreover, concentrating exclusively on early embryonic development renders the long-term consequences of EMF exposure during subsequent stages uncertain. Similarly, Chen et al. (2021) did not investigate the long-term effects of EMF exposure on fertility or reproductive outcomes beyond embryonic development. The short exposure time to EMF in the study by Kozlowska et al. (2021) resulted in insufficient long-term evidence on the effects of EMF exposure on endometrial function and overall fertility. In an interventional study conducted by de Vocht & Lee (2014), the exposure duration was 1 to 3 months, which may not adequately represent long-term effects. The majority of the animal studies focused on short-term impacts without addressing potential long-term or cumulative effects of EMF exposure (Poulletier de Gannes et al., 2013; Hafizi et al., 2014; Qi et al., 2015; Ahmadi et al., 2016; Alchalabi et al., 2016b; Khaki et al., 2016).

<u>Risk of bias</u>

Selection bias was identified in a prospective observational study by Tokinobu et al. (2021) due to unknown participation rate, while attrition bias was identified in a retrospective observational study by de Vocht et al. (2014) due to missing data on the residential addresses and maternal smoking status. Reporting bias was noted in two observational studies (Xu et al., 2016; Tokinobu et al., 2021) due to the high possibility of recall bias in self-reported questionnaires.

Theme 2: Measurement and instrumentation

<u>Validity threats</u>

According to Kozlowska et al. (2021), *in vitro* study was susceptible to inconsistent responses to EMF exposure due to the variations in the sensitivity of different genes and proteins towards EMF radiation. Meanwhile, interventional study by Vocht & Lee (2014) addressed the limitation of maintaining comparable conditions between the control and experimental groups, as confounding factors may still affect the results. A case-control study conducted by Sadeghi et al. (2017) omitted various confounding risk factors that could influence preterm birth, suggesting that the study's findings may not be generalisable to other populations or geographies. Mahmoudabadi et al. (2015) performed a case-control study to investigate the association between mobile phone usage during pregnancy and the risk of spontaneous abortion. Nonetheless, potential confounding variables, such as risk factors for spontaneous abortions, including balanced chromosomal abnormalities were not evaluated, and data on spontaneous abortions at very early stages were not recorded. Animal study by Woelders et al. (2017) observed differences among exposure units for certain measured parameters, which indicated that even small deviations in local climate conditions or mechanical factors can influence experimental outcomes. Residual confounding factors were identified as one of the primary limitations in retrospective, prospective and longitudinal observational studies (de Vocht et al., 2014; de Vocht & Lee, 2014 secondary data; Migault et al., 2018; Auger et al., 2019; Ingle et al., 2020; Tokinobu et al., 2021).

Limitations/variations in measurement methods

Several limitations with regards to the measurement methods were observed in the reviewed studies. In an interventional study conducted by Dias et al. (2023), participants' pregnancy and implantation rates were not evaluated, and gene expression analysis was limited. A case-control study by Sadeghi et al. (2017) investigating preterm birth in women residing within 600 meters of high voltage power lines had notable limitation, particularly in its measurement methodology. The study employed geographical information systems (GIS) to estimate proximity to power lines but failed to consider all sources of magnetic fields within the domestic setting. Furthermore, this study was unable to randomly allocate pregnant women to reside in proximity to or at a distance from the power lines. Mahmoudabadi et al. (2013) conducted a case-control study utilising a measurement device for ELF-EMF that encompassed a limited frequency range of 30 Hz to 3 kHz, possibly overlooking additional significant frequencies. In a case-control study conducted by Esmailzadeh et al. (2019) examining the correlation between exposure to EMFs from high voltage overhead power lines and female infertility, the EMF intensity in residential areas was not directly quantified using a low-frequency gauss meter; rather, the evaluation relied on the proximity to power lines.

Several animal studies mentioned limitations due to variability in experimental design across studies, such as differences in Specific Absorption Rate (SAR) values, frequencies, duration of exposure, and controlled environments, making it difficult to draw definitive conclusions (Poulletier de Gannes et al., 2013; Alchalabi et al., 2016b; Papoyan et al., 2018). Meanwhile, Saygin et al., 2018 faced variability in the oestrous cycle of animal models, affecting the determination of the exact stage of the cycle and influencing results. Other animal studies showed a limited scope of measurements; for example, (i) Wang et al. (2022) only investigated the effects of a single 60-minute exposure to 16 T HiSMF with 700 MHz RF-EMF, leaving out the effects of repeated or chronic exposure and acoustic noise effects, (ii) Burcu et al. (2020) did not examine the mechanisms that induce tissue-inducible nitric oxide synthase (iNOS) activity, (iii) Ruan et al. (2019) assessed only partial fertility parameters and (iv) Alchalabi et al. (2016a) did not fully elucidate the underlying mechanisms by which oxidative stress contributes to tissue damage, focusing instead on specific biochemical markers and histopathological changes without assessing other potential biomarkers or pathways.

Three studies employing retrospective and prospective observational designs exhibited methodological limitations resulting from misclassification of exposures and measures (de Vocht et al., 2014; de Vocht & Lee, 2014 secondary data; Li et al., 2017; Auger et al., 2019).

Theme 3: Contextual constraint

Applicability of findings

Three types of study design were found to have limitation with regards to applicability of the findings in humans. The use of porcine oocytes as a model in the *in vitro* study by Chen et al. (2021) may not fully represent human oocyte physiology and not fully mimic the complex interactions of the female reproductive system. According to two studies that conducted intervention study design using animal models (de Vocht & Lee, 2014; Rad et al., 2014), direct applications to humans are limited since animal models may not accurately depict human physiology and responses to electromagnetic fields. Similarly, three studies that conducted animal study designs addressed the limitation of applying findings to human fertility as laboratory conditions may not mimic natural environment (Ahmadi et al., 2016; Papoyan et al., 2018). Bakacak et al. (2015) further highlighted on the ethical concern that impedes the conduct of comparable experiments in humans.

Theme 4: Practical constraint

Resource constraint

Dias et al. (2023) conducted a prospective intervention study on the potential effects of EMF in women with diminished ovarian reserve undergoing assisted reproductive technology (ART) via clinical trials. However, there was lack of pregnancy outcome data, necessitating further research using a larger and randomised cohort. Meanwhile, interventional study by Rad et al. (2014) and animal study by Bakacak et al. (2015) highlighted the technical limitations that prevented the determination of ovarian follicle counts, as well as the lack of analysis on the destruction and apoptosis in harvested ovarian tissues.

Theme 5: Analytical constraint

Animal study by Woelders et al. (2017) included multiple comparison and interactions which could increase the likehood of false positives. Moreover, the dependence on parameters, such as initial egg weight influencing embryo weight, further complicated the interpretation of results. Three observational studies highlighted the analytical limitations, which include insufficient statistical power to detect associations (Tokinobu et al., 2021), failure to meet statistical test assumptions (Abad et al., 2016) and potential underpowering to detect associations with high exposure levels due to low prevalence of high exposures in the study population.

DISCUSSION

Planning a study design requires a thoughtful attention to various elements to ensure it is best suited the objectives of the study. This scoping review identified five prominent study designs utilised by researchers to assess the impact of EMFs on female fertility over the past 10 years: animal model, observational, interventional, case-control and *in vitro* studies. Given the influence that variations in research methodologies can have on the study outcomes, this review analysed the limitations of each study design via thematic analysis.

With regards to the operational limitation of various study designs, this review reported that short study duration and small sample size were the most frequently stated factor impacting the generalisability of the study findings. Previous studies have demonstrated that short study periods, particularly in longitudinal cohort studies, might have a negative impact on the statistical power and precision of regression coefficient estimations (Raudenbush & Xiao-Feng, 2001; Moerbeek, 2008). Therefore, a longer study period is beneficial for evaluating the long-term effects and gaining a more comprehensive understanding of the outcomes, as well as for identifying potential delayed effects (Collins & Graham, 2002). Nevertheless, increasing the length of the study period can be costly in terms of resources, finances, and time, while also imposing a considerable strain on participants about their prolonged commitment, potentially resulting in response fatigue. Furthermore, prolonged study duration may lead to higher participant attrition bias due to illness, death or loss of interest to continue participation (Raudenbush & Xiao-Feng, 2001; Collins & Graham, 2002; Moerbeek, 2008). Loss of participants to follow-up will subsequently reduce the sample size, introduce selection bias, and adversely affect the statistical power of the study (Kristman et al., 2003).

The articles reviewed in this study showed that the translation from animal studies to humans is the main limitation in study designs that involved animal model. Even though the use of animal research is necessary, particularly in testing the safety and effectiveness of new drugs before clinical trials (Sibbald, 2000), its use has been controversial. The applicability of animal experiment results to humans is debated mainly due to biological disparities between species, and poor methodological designs, conduct and analysis. According to Perel et al. (2007), diverse animal species and strains exhibit a range of metabolic pathways and drug metabolites, resulting in variability in efficacy and toxicity. Moreover, variations in drug dosing schedules, regimens and follow-up duration are of uncertain relevance to the human condition. The differences in laboratory techniques can influence outcomes, and small experimental groups result in insufficient statistical power.

Confounding factors were also observed as the main limitation in the majority of the study design reviewed. It is one of the common forms of bias present in observational studies evaluating the safety and effectiveness of treatments (Assimon, 2021). Confounding is described as a 'mixing effect' in which the effects of exposure being studied are conflated with those of surrounding factors, leading to a misinterpretation of the true relationship. The existence of confounding variables may mask an actual association making it difficult to establish a definitive causal relationship between treatment and the outcome (Skelly et al., 2012). Recognising potential confounding factors and mitigating their impact is essential for the study's credibility.

The diverse methodological parameters and measurement instruments utilised by researchers to evaluate the impact of EMF exposure on female fertility in the reviewed studies further posed an additional challenge for quality assessment. Heterogeneity in research methods may complicate the interpretation of results and hinder the replication of study designs in various contexts. In animal research, the implementation of standardised frequencies, intensities, and durations of exposure will enhance comparability across studies. Bleich et al. (2020) assert that the refinement and development of model-specific methodologies for evaluating impacts of treatments in animal studies, along with minimal or non-invasive monitoring and imaging techniques, can enhance data quality and improve ethical considerations.

Several limitations were identified across the reviewed studies. First, there was scarcity of research papers that specifically addressed the relationship between EMF exposure and female fertility, as opposed to those that addressed male fertility. Therefore, the inclusion criteria for the publication years spanned over a decade, from 2013 to 2023. Second, the screening process was impeded by the inability to access full text articles for several papers, affecting the comprehensiveness of the scoping review. Lastly, several relevant papers were excluded from the analysis due to their publication in languages other than English.

Future studies may conduct comparable research using more unified assessment criteria and a standardise definition of EMF exposure to enable replication of the study design and facilitate easier interpretation of findings. Well-designed *in vitro* or *in vivo* studies using animal models are essential to study the mechanisms and the effects that have been suggested in literature. Long-term EMF exposure and larger cohort studies are necessary to examine the detrimental effects emitted by the waves on female reproductive health, in order to enhance understanding of safety levels and the effectiveness of intervention strategies. Inclusion of diverse demographic groups and possible confounding factors will mitigate research bias, enhance the evaluation of EMF exposure implications, and improve the generalisability of the study findings. In addition, adequate financing and resources are essential for conducting extensive and long-term research.

CONCLUSION

This scoping review elucidates the present research designs and their prevalent methodological limitations in studies assessing the reproductive risks associated with low and high frequencies of EMFs. It is essential to recognise and address these limitations in order to preserve the credibility and integrity of research findings. Prospective cohort studies with comprehensive exposure assessments may represent the best research design for investigating the impact of EMF on female fertility. Such studies would enable the measurement of EMF exposure during aetiologically relevant periods and allow for the control of confounding factors while maintaining a longitudinal perspective on fertility outcomes. This review can serve as a guide for future researchers in developing effective intervention models by effectively navigating common limitations and enhancing the robustness and applicability of their contributions by adopting transparent reporting practices and implementing mitigation strategies.

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CONFLICT OF INTEREST

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Supplementary Table 1

Characteristics of articles reviewed: Types of study designs and study limitations

No.	Title	Author/s (Year)	Type of study design/Study duration/n	Study limitations
1.	Ozone sauna therapy and pulsed electromagnetic field therapy could potentially improve outcome in women with diminished ovarian reserve undergoing assisted reproductive technology	Dias et al. (2023)	Prospective interventional study/Each participant underwent two IVF cycles: Cycle 1 was performed before treatment with OST + PEMF, followed by 3 weeks of treatment (OST + PEMF twice a week). Cycle 2 was conducted after the treatment period./ 50 women (aged 39.7 ± 1.1 years) with Diminished Ovarian Reserve (DOR).	Generalizability Issues • Small sample size Duration and Scope • Lack of pregnancy outcome data • Limited assessment of gene expression • Need for further research with larger cohort and randomised trials
2.	Effect of low-frequency electromagnetic field exposure on oocyte differentiation and follicular development	Rad et al. (2024)	Interventional research (experimental study)/21 days of EMF exposure/ 30 pregnant female mice, which were divided into two groups of 15 mice each (experimental and control).	Generalizability Issues • Limited sample size of animals examined. • Animal experiment, limiting direct applicability to humans. Technical or Analytical Limitations • Technical limitations prevented determination of ovarian follicle numbers before the study. Measurement and Exposure Assessment Limitations • Destruction and apoptosis were not analysed in the extracted ovarian tissues. • Lack of detailed understanding of the underlying molecular mechanisms.
3.	Influence of Radiofrequency Electromagnetic Waves From 3rd-Generation Cellular Phones on Fertilization and Embryo Development in Mice	Suzuki et al. (2017)	In vitro experimental study/60 minutes exposure to RF-EMW/male and female B6D2F1 mice	Generalizability Issues • Short exposure time. Measurement and Exposure Assessment Limitations • Only investigates early embryonic development, and post-implantation development of embryos was not investigated. • Potential effects on oxidative stress and antioxidants
4.	Effects of electromagnetic field (EMF) radiation on androgen synthesis	Kozlowska et al. (2021)	In vitro experimental study/Gilts slaughtered on	Generalizability Issues • Short-term EMF exposure. Technical or Analytical Limitations

	and release from the pig endometrium during the fetal peri-implantation period		days 15–16 of pregnancy. Endometrial slices were pre-incubated for 2 hours and then exposed to EMF treatments for 2 or 4 hours/5 post-pubertal gilts (Sus scrofa f. domestica)	• Does not provide data on long-term effects of EMF exposure on endometrial function and overall fertility. • Inconsistent response to EMF exposure, indicating potential variability in the sensitivity of different genes and proteins to EMF radiation.
5.	Effects of electromagnetic waves on oocyte maturation and embryonic development in pigs	Chen et al. (2021)	In vitro experimental study/in vitro maturation (IVM) period of 42–44 hours for the oocytes/pre-pubertal gilts	Measurement and Exposure Assessment Limitations • Use of porcine oocytes as a model may not fully represent human oocyte physiology. • Not fully mimic the complex in vivo environment of the female reproductive system. Duration and Scope • Did not investigate the long-term effects of EMF exposure on fertility or reproductive outcomes beyond embryonic development.
6.	Maternal Proximity to extremely low frequency electromagnetic fields and risk of birth defects	Auger et al. (2019)	Observational study (Retrospective cohort study)/ 1989 to 2016 / 2,164,246 live-born infants in hospitals in Quebec, Canada	Measurement and Exposure Assessment Limitations • Inconsistent exposure assessment and misclassification of exposure. Confounding Factors and Bias • Presence of residual confounding factor. Generalizability Issues • Generalisability of the result. Measurement and Exposure Assessment Limitations • The biological plausibility of extremely low frequency electromagnetic fields as a cause of birth defects is uncertain.
7.	Maternal Residential Proximity to Sources of Extremely Low-Frequency Electromagnetic Fields and Adverse Birth Outcomes in a UK Cohort	de Vocht et al. (2014)	Observational study (Retrospective)/ from 1990 to 2009 (data analysis from 2004 to 2008) /265,926 singleton live births.	Measurement and Exposure Assessment Limitations • Exposure misclassification measurement. Confounding Factors and Bias • Bias due to missing data residential addresses and maternal smoking status for a portion of the population. • Residual confounding from socioeconomic factors, as well as other environmental exposures correlated with distance to EMF sources. • Lack residential history during the full pregnancy period. Generalizability Issues • Prevalence of women living close to ELF-EMF sources was low, limiting the generalizability of the findings to populations with similar exposure patterns.
8.	Maternal Use of Induction Heating Cookers During Pregnancy and Birth	Tokinobu et al. (2021)	Observational study (prospective cohort study)/	Confounding Factors and Bias • Selection bias due to participation rate is unknown.

	Outcomes: The Kyushu Okinawa Maternal and Child Health Study		April 2007 to March 2008/1,565 mother–child pairs.	• Participants was assessed via self-reported questionnaires, which may be subject to recall bias or misclassification of exposure. • Other confounding factors that were not accounted for. Technical or Analytical Limitations • Insufficient statistical power to detect associations.
9.	Residential proximity to electromagnetic field sources and birth weight: Minimizing residual confounding using multiple imputation and propensity score matching	de Vocht & Lee (2014)	Observational study (secondary data)/ 2004 to 2008/140,356 live singleton births	Confounding Factors and Bias • Residual confounding exists due to unmeasured or incomplete measured confounding factors. Measurement and Exposure Assessment Limitations • Exposure misclarification. • Use of postal code centroids to estimate residential proximity to EMF sources may introduce measurement error. Generalizability Issues • Limit the generalisability of the findings to other populations or time periods.
10.	Association of personal exposure to power-frequency magnetic fields with pregnancy outcomes among women seeking fertility treatment in a longitudinal cohort study	Ingle et al. (2020)	Observational study (Longitudinal cohort study)/2012 to 2018/119 women	Generalizability Issues • Small sample size. • Limit the generalisability of findings to the general population due to this cohort comprised subfertile women seeking fertility treatment at an academic clinic only. Confounding Factors and Bias • Possible confounding factors.
11.	Association between electromagnetic field exposure and abortion in pregnant women living in Tehran	Abad et al. (2016)	Observational study (Longitudinal study design)/ during pregnancy, with data collected across three trimesters/413 pregnant women	Generalizability Issues • Small sample size. Technical or Analytical Limitations • Variation in magnetic field (MF) level and daily activity patterns of participants not fully accounted. • Statistical tests assumptions not met. Confounding Factors and Bias • Lack of information on other potential confounding factors (age, familial marriage, and interpersonal conflicts).
12.	Health Effects of Electromagnetic Fields on Reproductive-Age Female Operators of Plastic Welding Machines in Fuzhou, China	Xu et al. (2016)	Observational study (cross-sectional study design)/does not specify the exact time period for data collection/529 participants aged 18 to 40 years	Confounding Factors and Bias • Potential for recall bias in self-reported symptoms and medical history. Generalizability Issues • Limited generalisability beyond Chinese female workers in shoe factories. • Hormone levels may vary due to diurnal and menstrual cycle variations, affecting interpretation of results. • Cross-sectional study limit interpretation of causal relationships. Measurement and Exposure Assessment Limitations • Exposure assessment based on single workday measurements may not reflect true cumulative exposures.

13.	Maternal cumulative exposure to extremely low frequency electromagnetic fields and pregnancy outcomes in the Elfe cohort	Migault et al. (2018)	Observational study (prospective birth cohort study)/ This cohort study will follow the children until they reach 20 years of age/ 18,040 families and 18,329 children enrolled	Generalizability Issues • Inability to consider exposure to other occupational hazardous factors due to lack of accurate data. Technical or Analytical Limitations • Limited ability to modify exposure estimates individually based on specific exposure characteristics. • Potential underpowering to detect associations with high exposure levels due to low prevalence of high exposures in study population. • Lack of individual exposure measurements; exposure assessment based on job characteristics and duration of work during pregnancy. • Berkson error introduced by use of group average exposure in place of individual values in exposure assessment. Confounding Factors and Bias • Potential for residual confounding despite inclusion of known confounders in analysis.
14.	Exposure to Magnetic Field Non-Ionizing Radiation and the Risk of Miscarriage: A Prospective Cohort Study	Li et al. (2017)	Observational study (prospective cohort study)/ duration of the study was based on the participants' pregnancies, with the primary focus being on miscarriage before 20 weeks of gestation/913 pregnant women	Measurement and Exposure Assessment Limitations • Challenges in accurately measuring Magnetic Fields (MF) exposure levels. Technical or Analytical Limitations • Difficulty in ascertaining MF exposure long after the relevant window of exposure has passed. • Prospective study design required to capture MF exposure during an etiologically relevant period. Measurement and Exposure Assessment Limitations • Misclassification of MF exposure possible if measurements not conducted on a typical day. • Use of subjective or surrogate measures for MF exposure in past studies may have led to misclassification and null findings. • Focus on studying MF effects on cancer in past studies may have exacerbated the problem of inaccurate exposure assessment. Confounding Factors and Bias • Lack of dose-response relationship observed for MF exposure levels above 2.5 mG, possibly due to a threshold effect.
15.	Preterm birth among women living within 600 meters of high voltage overhead Power	Sadeghi et al. (2017)	Case-control study/ February 2013 to December 2014/135 cases of singleton live spontaneous preterm birth	Measurement and Exposure Assessment Limitations • The measurement method used to measure distance to power lines using geographical information systems (GIS) that may not capture all sources of magnetic fields in the residence and distance of pregnant women living from the power lines. Confounding Factors and Bias

				• Other confounding factors that might influence preterm birth. Generalizability Issues • The findings may not be generalized to other populations or locations.
16.	Exposure to extremely low frequency electromagnetic fields during pregnancy and the risk of spontaneous abortion: a case-control study	Mahmoudabadi et al. (2013)	Case-control study/2012/ 116 participants	Measurement and Exposure Assessment Limitations • Covers a limited frequency range.
17.	Exposure to Electromagnetic Fields of High Voltage Overhead Power Lines and Female Infertility	Esmailzadeh et al. (2019)	Case-control study/February 2014 to December 2016/ 471 participants with no history of infertility	Generalizability Issues • Findings may be partly subjective as electromagnetic field strength in residential areas was not directly measured with a low-frequency gauss meter. The assessment was primarily based on distance from power lines. • Cross-sectional nature study design did not permit assessment of the temporal and thus potentially causal relation of the exposure and infertility.
18.	Use of mobile phone during pregnancy and the risk of spontaneous abortion	Mahmoudabadi et al. (2015)	Case-control study/Study duration is not explicitly stated/ 600 participants (292 cases + 308 controls).	Confounding Factors and Bias • Unknown risk factors for spontaneous abortions, such as balanced chromosomal abnormalities, not assessed. • Data about unknown spontaneous abortions at very early stages not collected. • Potential confounding factors not fully adjusted for, despite adjustments in logistic regression analyses. Technical or Analytical Limitations • Mechanisms underlying the effects of EMF on the risk of spontaneous abortions not well understood. • Cell phones may not be the only source of electromagnetic fields (EMF). Generalizability Issues • Case-control nature of the study implies caution in causal interpretations.
19.	Study of Potential Health Effects of Electromagnetic Fields of Telephone and Wi-Fi, Using Chicken Embryo Development as Animal Model	Woelders et al. (2017)	Animal study	Technical or Analytical Limitations • Differences observed among exposure units for certain measured parameters. This indicates that even small deviations in local climate conditions or mechanical factors can influence experimental outcomes. • Some measured parameters were not independent of each other, which could complicate the interpretation of results. • The statistical analysis includes multiple comparisons and interactions, which could increase the likelihood of false positives.
20.	Influence of Low-Intensity Electromagnetic Field on Some Biological Parameters of	Papoyan et al. (2018)	Animal study/ Spanned six rounds, with each incubation lasting 22	Generalizability Issues • Limited sample size number. • Observations limited to parental generation and three subsequent generations only. Duration and Scope

	Freshwater Crustaceans Daphnia magna Straus		days/900 chicken eggs incubated and studied	• Limited scope of EMF frequency, intensities or durations. Measurement and Exposure Assessment Limitations • Conducted under laboratory conditions that may not perfectly mimic natural environments.
21.	Evaluating the biological safety on mice at 16 T static magnetic field with 700 MHz radio-frequency electromagnetic field	Wang et al. (2022)	Animal study/14 days/ 48 male C57BL/6 mice (8 weeks old)	Duration and Scope • The study only examined the effects of a single 60-minute exposure to 16 T HiSMF with 700 MHz RF-EMF. It did not explore the effects of repeated or chronic exposure. • The study did not investigate the potential effects of acoustic noise generated during MRI scanning on mice, which is a known issue at high magnetic field strengths. • The paper suggests that further research is needed to assess the impact of 16 T MRI on the reproductive system, implying that this area was not covered in the current study. Generalizability Issues • The study exclusively used male mice, and therefore, the results might not be directly applicable to female mice.
22.	Histopathological changes associated with oxidative stress induced by electromagnetic waves in rats' ovarian and uterine tissues	Alchalabi et al. (2016a)	Animal study/ Two groups exposed to 1,800 MHz GSM-like RF for 30 days and 60 days/30 female Sprague Dawley rats (3 months old, 180 g).	Technical or Analytical Limitations • The study identifies oxidative stress as a contributor to tissue damage but does not fully elucidate the underlying mechanisms of DNA damage and follicular atresia. • The study focuses on specific biochemical markers (MDA, GSH-PX, MT) and histopathological changes, but does not investigate other potential biomarkers or pathways that could be involved in the observed effects.
23.	The effect of non-ionizing electromagnetic field with a frequency of 50 Hz in Rat ovary: A transmission electron microscopy study	Khaki et al. (2016)	Animal study/ The study duration is: Experiment 1: 8 weeks (3 weeks intrauterine + 5 weeks post-birth). Experiment 2: 13 weeks (3 weeks intrauterine + 10 weeks post-birth)/ 30 Wistar rats (300 ± 30 g, 3 months old).	Generalizability Issues • Limited sample size. Duration and Scope • Lack of Long-term Exposure Analysis.
24.	The impact of electromagnetic radiation (2.45 GHz,	Saygin et al. (2018)	Animal study/30 days (1 hour/day)/ 18	Generalizability Issues • Limited sample size.

	Wi-Fi) on the female reproductive system: The role of vitamin C		female Sprague Dawley rats	Measurement and Exposure Assessment Limitations • Short and variable oestrous cycle in rats was noted as a challenge in determining the exact stage of the cycle, which could affect the results.
25.	Different periods of intrauterine exposure to electromagnetic field: Influence on female rats' fertility, prenatal and postnatal development	Alchalabi et al. (2016b)	Animal study/3 weeks exposure duration/ 60 virgin female Sprague-Dawley rats	Measurement and Exposure Assessment Limitations • The lack of consistency across different studies in terms of SAR values, frequencies, duration of exposure, and whether the exposure was short-term or long-term. Technical or Analytical Limitations • Limited understanding of precise biological mechanism. Generalizability Issues • Controlled environment may not fully replicate real-world scenarios of EMF exposure.
26.	The Effect of Extremely Low Frequency Pulsed Electromagnetic Field on In Vitro Fertilization Success Rate in NMRI Mice	Hafizi et al. (2014)	Animal study/The main experimental exposure (ELF-PEMF) lasted 5 hours. The entire process, from hCG injection to fertilization assessment, spanned 3 days/ 10 female and 2 male NMRI mice	Generalizability Issues • Small sample size used. Duration and Scope • Lack of long-term assessment.
27.	Rat fertility and embryo fetal development: Influence of exposure to the Wi-Fi signal	Poulletier de Gannes et al. (2013)	Animal study/ Male and female rats were exposed for a total of 6 and 5 weeks, respectively/ 12 pairs of animals per group (12 males and 12 females for each exposure condition).	Measurement and Exposure Assessment Limitations • Short exposure duration. • Only specific SAR levels used.
28.	The effects of prenatal and postnatal exposure to electromagnetic field on rat ovarian tissue	Burcu et al. (2020)	Animal study/ 9 weeks/8 pregnant Sprague-Dawley rats	Technical or Analytical Limitations • Does not examine the mechanisms that induce iNOS activity and how these mechanisms function. • The relationship between oxidative stress, the proinflammatory system, and iNOS activation due to EMF exposure was not thoroughly explored. Measurement and Exposure Assessment Limitations

				• Other potential impacts or compare with different EMF strengths and durations were not fully explored.
29.	Power-frequency magnetic fields at 50 Hz do not affect fertility and development in rats and mice	Ruan et al. (2019)	Animal study/rats were exposed for 24 weeks to PF-MF and mice were exposed for 12 weeks in the PF-MF/ 120 adult Sprague-Dawley rats and 64 C57BL/6J mice	Measurement and Exposure Assessment Limitations • Only assess partial fertility parameters.
30.	Effects of extremely low-frequency electromagnetic fields (ELF-EMF) exposure on B6C3F1 mice	Qi et al. (2015)	Animal study/15.5 months/Exposed Group: 10 pregnant females, resulting in 66 offspring (24 males, 42 females). Control Group: 10 pregnant females, resulting in 62 offspring (30 males, 32 females).	Generalizability Issues • Small sample size. • Primarily relies on observational analysis of outcomes in exposed and control groups of mice. It cannot establish causation or elucidate underlying mechanisms. Measurement and Exposure Assessment Limitations • Limited Duration of exposure.
31.	No adverse effects detected for simultaneous whole-body exposure to multiple-frequency radiofrequency electromagnetic fields for rats in the intrauterine and pre- and post-weaning periods	Shirai et al. (2017)	Animal study/ 8 weeks/ 14 pregnant Sprague-Dawley (SD) rats	Generalizability Issues • Primarily relied on observational analysis of outcomes in exposed and control groups. Confounding Factors and Bias • Functional development, water-maze, and behavioural tests were conducted after RF EMF exposure rather than in real-time exposure, which may introduce confounding variables.
32.	Effect of non-ionizing electromagnetic field on the alteration of ovarian follicles in rats	Ahmadi et al. (2016)	Animal study/ 8 weeks (Group 1: 3 weeks intrauterine + 5 weeks ectopic) or 13 weeks (Group 2: 3 weeks intrauterine + 10 weeks ectopic)/30 rats	Generalizability Issues • Animal model used may not fully represent human physiology and response to EMF exposure. • Limited sample size and duration of exposure. • Findings may not be directly applicable to human reproductive health. Measurement and Exposure Assessment Limitations • Lack of direct measurement of physiological parameters related to fertility. Confounding Factors and Bias • Potential confounding factors not fully controlled.

33.	The effects of electromagnetic fields on the number of ovarian primordial follicles: An experimental study	Bakacak et al. (2015)	Animal study/15 days /16 female Wistar-Hannover albino rats	Technical or Analytical Limitations • Technical difficulties prevented determination of ovarian follicle numbers before the study. • Destruction and apoptosis were not analysed in the extracted ovarian tissues. Generalizability Issues • Small sample size of rats examined. • Ethical concerns prevent conducting similar experiments in humans. Confounding Factors and Bias • Lack of pre-intervention ovarian primordial follicle (PF) numbers in experimental objects.